

**METHODS AND COMPOUNDS FOR MODULATING NUCLEAR RECEPTOR
COACTIVATOR BINDING**

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ABSTRACT OF THE DISCLOSURE

The present invention relates to methods and agonist/antagonist compounds for modulating
15 nuclear receptor coactivator binding. The invention includes a method for identifying residues
comprising a coactivator binding site for a nuclear receptor of interest. Also included is a method
of identifying agonists and/or antagonists that bind to a coactivator binding site of a nuclear
receptor of interest. Agonists and antagonists of coactivator binding to nuclear receptors also are
provided. The invention is exemplified by identification and manipulation of the coactivator
20 binding site of the thyroid receptor (TR), and compounds that bind to this sites. The methods can
be applied to other nuclear receptors including RAR, RXR, PPAR, VDR, ER, GR, PR, MR, and
AR.